REMARKS

I. Interview Summary

The Applicants thank Examiner Jeffrey Lundgren for the courtesy of a telephonic interview on April 5, 2006 with the Applicants' attorneys David A. Gass and Sharon M. Sintich. During the interview, the petition pursuant to 37 C.F.R. §1.181 and §1.144 to request review and withdrawal of a 442-way restriction requirement, which was filed in parent application no. 09/908,943, was discussed. A copy of the Petition Decision issued by the U.S. Patent and Trademark Office is attached hereto as Exhibit A. The Applicants traverse the current restriction requirement and, as one option for its replacement, request that the Petition Decision be applied to the pending claims.

During the interview, the Applicants requested that the Petition Decision be applied to the pending claims. In particular, the Examiner stated that he was amenable to the election of a four amino acid peptide in view of the foregoing amendment. The Examiner also stated he would consider withdrawing the portions of the outstanding restriction requirement that were inconsistent with the Petition Decision.

Also as discussed during the interview, the generic claims have been amended to a similar format to the currently pending claims in parent application no. 09/908,943. In the parent application, the Applicants have argued that the generic claims are patentable. It is premature for the Applicants to know the status of the parent claims at the time of election in the present application. The Applicants do not intend to pursue issuance of claims of identical scope in more than one patent.

II. Support for Amendments

The amendment to the specification to insert several paragraphs of text finds support in U.S. patent application no. 09/416,901 (now U.S. Patent No. 6,699,674) at page 9, line 19, through page 10, line 12, at page 33, line 7-23 and at page 50, line 20, through page 51, line 12. This patent application is incorporated by reference in its entirety in the present application (see page 39, lines 26-27). Therefore, insertion of these paragraphs does not add new matter to the specification pursuant to 37 C.F.R. 1.57(c).

The paragraphs inserted by the foregoing amendment refer to the sequences of SEQ ID NO: 198 and 199. A substitute sequence listing is submitted herewith to include these sequences. This amendment does not add new matter because the sequences were disclosed in the parent application no. 09/416,901, which is incorporated by reference in its entirety in the patent application as described above.

A number of the claims contain limitations defining the beta secretase polypeptide used in methods of the invention. These claim recitations are described in the specification at page 39, line 18 through page 42, line 6, including the paragraphs newly introduced from the application that is incorporated by reference. (In addition, these polypeptides and polynucleotides are claimed in related U.S. Patent Nos. 6,828,117, 6,825,023, 6,737,373, 6,797,487, 6,753,163, 6,867,018 and 6,913,918.)

The new claims are supported through out the specification and do not add new matter to the application. In particular, β-secretase polypeptides purified and isolated from a cell transformed or transfected with a polynucleotide encoding the polypeptide and is supported at page 9, lines 17-21. Methods of administering a test agent to a non-human mammal and is supported at page 67, lines 18-26. Substrates that are expressed in a cell transformed or transfected with a polynucleotide encoding that substrate are supported at page 43, line 23, through page 44, line 14.

Claims 1-42, 50-57, 61-62, 65 and 67-83 are canceled without prejudice because these claims were directed to unelected inventions. Applicants reserve the right to purse claims of the same or similar subject matter in continuing applications.

III. Election

Pending claim 1, 4-6, 14-28, 36, 38, 41, 43, 49, 52, 58-60, 63, 64, 66, 70 and 72-83 were restricted into the following groups of inventions. The Applicants were required to elect (1) a particular type of invention, (2) a particular peptide species used in or referred to by the invention and (3) a particular aspartyl protease used in or referred to by the invention.

A. Group I consists of claims 1, 4-6, 14-28, 70 and 72-83 drawn to compositions comprising isolated polypeptides having the general formula $P_3P_2P_1 - P_1'P_2'P_3'$.

B. Group II consists of claims 36, 38, 41 and 52 drawn to a polynucleotide, vector, host cell and method of expressing a polypeptide in a host cell.

C. Group III consists of claims 43, 49, 58-60, 63, 64 and 66 drawn to methods of assaying the activity of proteins in the presence of peptides having the general formula $P_3P_2P_1 - P_1'P_2'P_3'$.

Applicants hereby elect the invention drawn to methods for assaying for the activity of proteins in the presence of peptides having the general formula $P_2P_1 - P_1'P_2'$ (Group III) using a substrate comprising the peptide having the particular amino acid sequence NF-EV and the aspartyl protease having the amino acid sequence of SEQ ID NO: 2.

IV. Traversal of Election of a Single Peptide Sequence

In the Office Action, the Examiner required election of a single peptide sequence $P_3P_2P_1 - P_1'P_2'P_3'$. As discussed in the interview, the claims are amended to recite substrates comprising a peptide having an amino acid sequence of at least 6 amino acids wherein the four amino acids defined by formula P_2P_1-$P_1'P_2'$ are particularly defined (P_2 is N, P_1 is F, P_1' is E and P_2' is V). At pages 9-10 of the attached Petition Decision, Director Kisliuk required that Applicants elect a peptide having the formula P_2P_1-$P_1'P_2'$ wherein P_2, P_1, P_1' and P_2' are each selected from the amino acid residues set out in the Table 1. For the Examiner's convenience, Table 1 is reproduced below:

P2	P1	P1'	P2'
N	Y	E	V
L	L	A	A
K	M	D	N
S	Nle	M	T
G	F	Q	L
T	H	S	F
D		G	S
A			
Q			
E			

The Applicants request that requirement to designate a core sequence of a peptide species as part of the election be limited to four amino acids rather than six amino acids as stated in the restriction requirement. The election of a four amino acid species is consistent with the attached Petition Decision. In addition, a search based on the four amino

acid species is not unduly burdensome. Even if the computer-based sequence search based on the elected substrate peptide sequence identifies a large initial pool of literature, the pool can be expected to be easily reduced (or completely eliminated) in the context of additional limitations of the elected method claims. In the absence of a teaching or suggestion in the prior art to use a peptide as a substrate for an aspartyl protease as recited in the method claims, the claims will be novel and unobvious. The ability to limit the peptide search with other search parameters greatly lessens the burden perceived by the Examiner.

V. Traversal of Election of a Single Aspartyl Protease

The Examiner required election of a single aspartyl protease (SEQ ID NO: 2 or SEQ ID NO: 4). The amino acid sequences of SEQ ID NO: 2 and SEQ ID NO: 4 are identical except for a 25 amino acid insertion/deletion in one sequence relative to the other. Thus, the two sequences are putative splice variants that arise from the sequence, with 476 common amino acid residues which form various common functional domains (*e.g.*, signal sequence, pro-peptide, DTG/DSG active site tri-peptide motifs, transmembrane domain, etc.).

It would not be unduly burdensome for the Examiner to search both aspartyl proteases. The numerous Gurney *et al.* β-secretase patents that have already issued to the assignee of this application disclose both the long and short form splice variants of human β-secretase, as well as murine β-secretase, in a single document. (See, *e.g.*, any of Gurney *et al.*, U.S. Patent Nos. 6,699,671; 6,828,117; 6,825,023; 6,737,510; 6,797,487; 6,753,163; 6,867,018; 6,844,148; 6,835,565; 6,790,610; 6,727,074; 6,706,485; 6,500,667; 6,440,698; and 6,420,534.)

Taking Patent No. 6,844,148 as an example, not only does the specification describe the human long and short form of β-secretase, murine form, and active variants thereof, but the claims are directed to secretase assays that involve use of SEQ ID NO: 2, variants thereof (*e.g.*, 95% identity, transmembrane deletion fragments, N-terminal and C-terminal deletion fragments, cell-free and cell-based assays, and use of multiple substrates). This is direct evidence that neither search nor examination require undue burden.

Because SEQ ID NOS: 2 and 4 are related sequences wherein SEQ ID NO: 4 has a deletion of 25 amino acids at residue 190, relative to SEQ ID NO: 2, but the sequences otherwise comprise long stretches of identical sequence, any computerized sequence-based

search will uncover all art related to either sequence. For this reason too, a search based on both β-secretase polypeptides is not unduly burdensome, and the election requirement should be withdrawn.

CONCLUSION

In view of the foregoing remarks, Applicants respectfully request that the restriction requirement be withdrawn.

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Respectfully submitted,

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